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Depression and panic disorder as predictors of health outcomes for patients with asthma in primary care

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Summary
Introduction: Depression and panic disorder are widely acknowledged as complicating factors in asthma patients. However, their impact on health outcomes in primary care patients is less well examined. This study prospectively evaluated the impact of depression and panic disorder on outcomes of primary care patients with asthma over 1 year.
Methods: At baseline, 256 asthma patients from 43 primary care practices completed self-report questionnaires including the Patient Health Questionnaire (PHQ), the Asthma Quality of Life Questionnaire (AQLQ), and a structured questionnaire evaluating asthma severity, hospitalisation and emergency visits. One year later, 185 (72.3%) patients completed the same questionnaire.
Results: At baseline, 3.9% of patients suffered from major depressive disorder, 22.7% from minor depressive disorder, and 7.8% from panic disorder. In the year under evaluation, 17 patients (9.2%) received emergency home visits and 10 patients (5.4%) were admitted to a hospital. Depression at baseline predicted hospitalisation within the subsequent year (OR 6.1; 95% CI 1.5–24.6) and panic disorder predicted unscheduled emergency home visits (OR 4.8; 95% CI 1.3–17.7). Depression but not panic disorder predicted the AQLQ scales activity ($p = 0.001$), symptoms ($p = 0.001$), emotions ($p = 0.001$) and environment ($p = 0.001$) at follow-up.
Conclusions: Although rates of hospitalisation and emergency visits in primary care are low, the impact of psychiatric comorbidity on health outcomes for patients with asthma is substantial. It might be helpful to identify patients with psychiatric comorbidity by analysing reasons for hospitalisation and emergency visits. For these patients, intensifying

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care with psychiatric interventions might help to reduce inappropriate healthcare utilisation and avoid adverse outcomes.

Introduction

Asthma is a common chronic disease with a high prevalence of approximately 5% in industrialised nations. It is characterised by a chronic inflammation process which induces bronchial hyper-responsiveness and reversible airway obstruction.[1] Asthma is therefore acknowledged widely as an organic disease. This cannot be taken for granted as it was historically seen as a purely psychosomatic disease.[2] Since then, more complex models have emerged which describe asthma as an organic disease with a high vulnerability to psychological influences.[2,3] It was demonstrated using a telephone survey that asthma patients had a higher risk for anxiety or depression.[4] A high psychiatric comorbidity was shown especially for patients with severe or difficult asthma.[5,6] A recent cross-sectional survey showed an association between depression and lifetime hospital visits in asthma patients.[7] In a prospective trial, anxiety/depression predicted a higher hospitalisation rate in patients initially presenting with exacerbation of asthma or COPD.[8] In contrast, Greaves et al. found in patients with recent asthma attacks that low panic fear and high control confidence was associated with an increased risk of asthma attacks within 12 months.[9] This was attributed to a lower self-awareness with respect to the disease for these instable patients. However, these prospective surveys were performed with highly selected patients from emergency departments or hospitals. Thus, the impact of psychiatric comorbidity on the long-term outcome of patients with asthma in primary care remains unclear. This is important, as unselected patients in general practice present with all levels of asthma severity, with a higher preponderance of mild or moderate courses of disease[10,11] which are influenced by psychological factors to an unknown extent. Therefore, the aim of this prospective study was to evaluate the impact of depression and anxiety on health care utilisation outcomes and quality of life in general practice asthma patients over 1 year.

Methods

Study design

This longitudinal survey was performed in Saxony–Anhalt with asthma patients from 46 general practices (GPs). The participating general practices were involved in a quality improvement project, which was financed by the Ministry of Health (ISRCTN51102813).

Setting and patients

GPs were asked to hand out a questionnaire to each patient with asthma coming for consultation between May and July 2005 (beginning of study, t1). All GPs were instructed via a leaflet to select patients on basis of previously performed diagnostics such as spirometry or broncho-provocation. Additionally, the most relevant criteria to distinguish between asthma and COPD were explained in the leaflet, e.g. they were instructed to preferably select patients with varying symptoms, attacks of dyspnoea and wheezing or with a known allergy. Heavy smokers likely to have COPD were to be avoided. Patients were asked to complete the questionnaire and to send it to the study centre, assuring the anonymous handling of their data. Three prizes of 250€ were raffled as an incentive for the patients' participation. One year later, on 1 June 2006 (t2), the patients received the same questionnaire posted from the study centre. Again, three prizes of 250€ were raffled as an incentive. Three reminders were sent out after 4, 8 and 12 weeks. The study was approved by the Medical Ethics Committee of the Medical Faculty at the University of Heidelberg.

Measures

The presence of major and minor depressive disorders as well as panic disorder was established according to DSM-IV diagnostic criteria using the validated German version of the Patient Health Questionnaire (PHQ).[12,13] The nine-item depression module evaluates the presence of one of the nine DSM-IV criteria for major depression. Major depression is diagnosed when five or more questions are answered with 'symptoms on more than half of the days'. Minor depression is diagnosed when two, three or four questions are answered with 'symptoms on more than half of the days'. The question 'Thoughts that you would be better off dead, or of hurting yourself in some way?' is included when the response 'On several days' is endorsed. The panic disorder module comprises five items. According to DSM-IV diagnostic algorithms, panic disorder is diagnosed when all five PHQ items are answered positively. Excellent operating characteristics have been demonstrated for the American[14,15] and German versions of the PHQ.[12,13] It has also been shown that the PHQ diagnostic algorithms result in realistic estimates of base rates for major depressive disorder, and panic disorder.[16] With reference to a gold standard interview for mental disorders, the sensitivity of the PHQ classification for major depressive disorders is 83% and its specificity is 90%,[13] for panic disorder its sensitivity is 86% and its specificity is 91%.[12]

To determine the patients' health-related quality of life, the standardised German version of the 'Asthma Quality of Life Questionnaire' (AQLQ) was used. The AQLQ, which has strong measurement properties,[17] has 32 items on a seven-point scale and measures four dimensions of health-related quality of life (QoL), namely activities, symptoms, emotions and environment. These four dimensions are summarised in an overall score. The range of all scales, including the sum score, is from 1 (worst) to 7 (best), the minimal important change is 0.5.[18] The AQLQ measures have been shown to be

related to the clinical status of the asthma.[19] Patients were asked about their daily and nocturnal asthma-related symptoms according to the international levels of asthma severity (intermittent, mild persistent, moderate persistent, severe persistent).[20] Current medication including dosage was documented by the patient in a structured register. Additionally, patients were asked if they had been admitted to hospital within the last 12 months due to their asthma (if admitted: how many days in hospital) and if they had received unscheduled home visits by a GP or ambulatory care due to their asthma within the last 12 months (if received: how often).

Analysis

Questionnaires were scanned and data were imported automatically into SPSS 14.0 by Eyes & Hands® Forms, Version 5. Baseline data were presented descriptively. Differences between females/males and responders/non-responders were calculated using *t*- or χ^2-tests as appropriate. To assess adherence to guidelines, each patient's medication was checked manually. Full adherence to guidelines implied that the prescribed medication was consistent with the guidelines and that the patient had intermittent or mild persistent asthma for day and night.[20] Full adherence was also recorded when the patient suffered from moderate of severe persistent asthma but received end-of-dose therapy such as oral steroids. Guideline adherence, but under-dosing of medication implied that a patient receiving appropriate medication presented symptoms indicative of moderate or severe persistent asthma such that the dose needed to be increased. Inappropriate prescribing of medication implied that the patient had not been treated according to guidelines, e.g. if only sympathomimetics without steroids were prescribed in mild, moderate or severe persistent asthma. Odds ratios related to hospitalisation (yes/no) and unscheduled emergency visits (yes/no) at follow-up were estimated with univariate logistic regression using the diagnoses of any depressive disorder (i.e. major and minor depressive disorder) and panic disorder as independent variables. Odds ratios were also calculated for asthma severity, sex, age, smoking habits, inhaled steroids and inhaled sympathomimetics and medication guideline adherence in order to control for the factors most affecting asthma outcome. A logistic regression model (backward selection) was calculated with hospitalisation/unscheduled emergency visits as dependent variables and depression, anxiety, medication guideline adherence, sex, age and smoking habits as independent variables to determine the strongest predictors. An ANCOVA model with either depression (t1) or panic disorder (t1) as covariate and severity of asthma (t2) as a fixed factor was established to predict quality of life at 12-month follow-up (t2). Medication guideline adherence, sex, age and smoking habits were included as fixed factors to control for the factors most relevant to asthma outcome.

Results

Baseline characteristics

A total of 314 patients received the questionnaire from their GPs. Two hundred and fifty-six patients (response rate: 81.5%) sent back the questionnaire. One hundred and fifty-eight of the responders were female (61.7%); and the average age (S.D.) was 56.3 (16.4) years. At baseline, there was no significant difference between responders and non-responders with regard to age, sex and asthma severity (non-responder analysis not in the table). Nearly half of the patients reported symptoms corresponding to moderate or severe persistent asthma as they had daily symptoms (Table 1). We found high psychiatric comorbidity in the asthma patients with 7.8% suffering from panic disorder and 26.6% fulfilling the criteria for major or minor depressive disorders. We found no difference between depressed and non-depressed patients with respect to age ($p = 0.192$; *t*-test) or sex ($p = 0.194$; χ^2-test). The use of steroids was relatively high, with 68.8% receiving inhaled and 8.2% oral steroids. Only 27% of the patients participated in an educational asthma program. Forty percent received medication with full adherence to guidelines, 34% were treated according to guidelines, but with a dosage which was too low and suffered from moderate or severe asthma. Twenty-one percent received inadequate medication.

Table 1 Baseline patient characteristics ($n = 256$).

Age	Mean (S.D.)
	56.3 (16.4)
Asthma severity	*N* (%)
Intermittent	59 (23.0)
Symptoms less than once a week	
Mild persistent	
Symptoms more than once a week, less than once a day	63 (24.6)
Moderate persistent	
Symptoms daily, but not continuously	92 (35.9)
Severe persistent	
Symptoms continuously, limitation to physical activities	19 (7.4)
Medication	
Inhaled steroids	176 (68.8)
Oral steroids	21 (8.2)
Inhaled sympathomimetics	200 (78.1)
Full medication guideline adherence	103 (40%)
Medication guideline adherence, but underdosing	80 (34%)
Inadequate medication	50 (21%)
Self management	
Asthma education	69 (27.0)
Smoking	65 (25.4)
Psychiatric comorbidity (PHQ)	
Major depression	10 (3.9)
Minor depression	58 (22.7)
Panic disorder	20 (7.8)

PHQ: Patient Health Questionnaire.

Twelve month follow-up

One hundred and eighty-five patients (72.3%) responded to the follow-up survey 1 year later. The responders and

non-responders at follow-up (t2) did not differ with respect to sex and age. There was also no significant difference with respect to asthma severity at t1 between responders and non-responders at follow-up ($p = 0.12$ in χ^2-test; not shown in the table). Quality of life declined and depression increased with asthma severity (Table 2). The ANOVA was significant with respect to these differences. Asthma severity improved moderately from t1 to t2. This might be due to the GPs meetings in quality circles, where they attended educational meetings to reflect optimal asthma care under the guidance of a trained facilitator.[21] However, there were no significant changes in quality of life and depression scores within 1 year.

Predictors of hospitalisation and unscheduled emergency visits by GPs at 12 months

Ten patients were hospitalised during the 1-year follow-up time, with an average length of stay of 15.2 days (S.D. 12.5; min 1; max 40), eight were male (12% of all males) and two were female (2% of all females). Seventeen patients received unscheduled emergency visits from their GPs, with an average frequency of 3.1 (S.D. 2.50; min 1, max 10). Hospitalisation was predicted by depressive disorder, asthma severity at t1 and sex (Table 3). The logistic regression, including interaction analysis showed no interaction between asthma severity and depressive disorder. There was also no significant interaction between sex and asthma severity, depression, anxiety, medication guideline adherence or smoking. In the logistic regression model (backward selection), which controlled for medication guideline adherence, smoking, age and sex, only depressive disorder ($p = 0.009$) and sex ($p = 0.008$) remained significant predictors for hospitalisation (data not in table). Unscheduled emergency visits were predicted by panic disorder at t1, asthma severity and medication guideline adherence (Table 3). The logistic regression with interaction analysis showed no interaction between asthma severity and panic disorder. In the logistic regression model (backward selection), which controlled for medication guideline adherence, smoking, age and sex, only panic disorder remained a significant predictor for unscheduled emergency visits ($p = 0.050$). Besides that, patients with asthma education had more emergency visits ($p = 0.024$). Indeed patients with asthma education also suffered from more unfavourable

Table 2 Quality of life and depression scores at baseline (t1) and follow-up (t2) ($n = 185$).

Asthma severity	t1			t2		
	N (%)	AQLQ,* Mean (S.D.)	Depression,† Mean (S.D.)	*N* (%)	AQLQ,* Mean (S.D.)	Depression,† Mean (S.D.)
Intermittent	46 (24.9)	5.48 (0.96)	4.20 (3.64)	47 (25.4)	5.62 (0.96)	3.83 (3.88)
Mild persistent	40 (21.6)	4.64 (0.94)	5.64 (4.05)	54 (29.2)	4.58 (0.86)	6.74 (5.21)
Moderate persistent	73 (39.5)	3.81 (0.98)	7.59 (4.90)	58 (31.4)	3.65 (1.0)	8.31 (5.10)
Severe persistent	15 (8.1)	3.20 (0.78)	8.33 (4.35)	19 (10.3)	3.16 (0.84)	9.38 (4.92)
Sum	174 (94.1)	4.44 (1.23)	6.17 (4.65)	178 (96.2)	4.47 (1.30)	6.59 (5.17)

AQLQ: Asthma Quality of Life Questionnaire; PHQ: Patient Health Questionnaire.
*Quality of life scores differ significantly between the different asthma severities ($F = 50.1$; $p < 0.001$).
†Depression scores (PHQ) differ significantly between the different asthma severities ($F = 9.6$; $p < 0.001$).

Table 3 Predictors of hospitalisation and unscheduled emergency visits within following 12 months (univariate logistic regression analyses).

Predictor	Hospitalisation (yes/no) (t2)			Emergency visit (yes/no) (t2)		
	OR	95% CI	*p*	OR	95% CI	*p*
Depressive disorder t1 (PHQ) (yes/no)	6.1	1.5–24.6	0.011	1.7	0.6–4.9	0.295
Panic disorder t1 (PHQ) (yes/no)	3.5	0.7–18.3	0.145	4.8	1.3–17.7	0.019
Asthma severity t1	2.6	1.1–6.2	0.035	3.5	1.6–7.5	0.001
Inhaled steroids	1.5	0.3–7.2	0.629	1.2	0.4–3.9	0.769
Inhaled sympathomimetics	2.0	0.2–16.6	0.509	3.7	0.5–29.1	0.213
Guideline adherence of medication (yes/no)	0.6	0.1–2.3	0.426	0.2	0.1–0.9	0.033
Gender	7.4	1.5–36.2	0.013	1.2	0.4–3.4	0.690
Age	1.0	0.9–1.1	0.592	1.0	0.9–1.0	0.781
Smoking	1.2	0.3–5.0	0.776	1.2	0.4–3.6	0.752
Asthma education (yes/no)	2.3	0.6–8.2	0.211	3.4	1.2–9.7	0.024

PHQ: Patient Health Questionnaire; depressive disorder is both minor and major depression.

asthma severity (OR 1.3; 95%.CI 0.9–1.8; $p = 0.098$; not in table).

Predictors of quality of life at 12 months

The ANCOVA with depression (t1) as covariate and asthma severity (t2), medication guideline adherence (t2), smoking habits (2), age and sex as a fixed factors showed a significant influence of depression (t1) and asthma severity (t2) on the scales of the AQLQ (Table 4 and Figure 1). The other control factors did not show any influence with the exception of a negative correlation between age and activity ($p = 0.005$). Panic disorder (t1) had no significant influence on the AQLQ scales. The asthma severity at t2 was the strongest predictor for quality of life. As illustrated in Figure 1, patients with depression at t1 reported lower health-related quality of life across all asthma severities at t2.

Discussion

Our study identified depression as a predictor of hospitalisation and panic disorder as a predictor of unscheduled emergency visits in primary care patients with asthma. Depression but not panic disorder at baseline predicted quality of life at follow-up.

Depression in particular is known as a predictor of health outcomes in several conditions such as cerebrovascular disease,[22] coronary heart disease,[23] and diabetes.[24] Its ability to influence somatic conditions also draws attention to asthma.[3,25,26] The origin of the independent predictive value of depression in our study remains speculative. Depressive symptoms were found to be a reason for poor adherence to asthma therapy,[26–28] which might lead to a higher hospital admission rate. A meta-analysis revealed that there might be a general relation between depression and poor adherence to therapy in chronically ill patients, which could be due to reduced cognitive functioning, negative expectations about the benefits of treatment and lower social support.[29] Besides that, it is speculated that depression itself could have a direct effect on airway instability and asthma exacerbation by directly influencing vagal activity[30] or its influence could be mediated by pathway defects in the function of the autonomic nervous system.[31]

Similar pathophysiologic pathways are known with regard to the course of disease in asthma and panic disorder[31]; and the relation between panic disorder and asthma is a well-known phenomenon.[33,34] Consistent with these previous findings, the prevalence of 7.8% of patients suffering from panic disorder in our study is much higher than in the general population (1.5%)[35] and comparable with prevalence rates in patients with pulmonary hypertension[36] and the results of an epidemiologic asthma survey.[37] We found that the presence of panic disorder had a strong and independent impact on unscheduled emergency visits by patients. A vicious cycle linking asthma severity, experience of asthma attacks and subsequent conditioning with hyperventilation and other panic symptoms,[32,38] might be responsible for frequent utilisation of home/emergency visits. Interestingly, Kullowatz et al. also found hospitalisation to be related to depression but not panic disorder in their cross-sectional survey.[7] However, this was based on retrospective lifetime hospital visits. It could be hypothesised that patients with panic disorders are treated by their GPs who prevent hospitalisation with their interventions. This might explain why we could not find panic disorder to influence hospitalisation. The strong influence of sex on hospitalisation remains unclear as there was no association with other factors such as depression, asthma severity or smoking. The evidence for the influence of sex on the course of disease is increasing[39] and was already found in COPD[40,41] and cardiovascular diseases.[42,43] Our study indicates that asthma might be more prevalent in women and suggests the presence of sex differences in morbidity risk for this disease as well. However, these results are due to secondary analyses. Therefore, further surveys including sex-related analyses would be necessary to confirm our findings. The positive association between asthma education and unscheduled emergency visits might be explained by the more unfavourable asthma severity of these patients.

Another important finding is that depression at baseline predicted quality of life at follow up, whereas panic disorder had no influence on this variable. Rimington et al. demonstrated the complex relation between depression, anxiety and asthma morbidity.[25] They found that depression and anxiety scores could help to explain symptoms over and above the effects of lung function. They concluded that reported symptoms may reflect not only 'hard measures' like FEV_1 but also non-asthma factors. Rosenzweig et al. also found that objective FEV_1 measures do not fully account for health related quality of life.[44]

Therefore, quality of life needs to be interpreted not only based on 'somatic' asthma severity but also based on

Table 4 Predictors of quality of life (ANCOVA with asthma severity at t2 as fixed factor and depression/anxiety as covariates).

Predictor	Activity t2		Symptoms t2		Emotions t2		Environment t2	
	F	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Depressive disorder t1 (PHQ) (yes/no)	12.14	0.001	11.25	0.001	6.96	0.009	10.11	0.002
Asthma severity t2	31.99	<0.001	42.82	<0.001	35.99	<0.001	27.20	<0.001
Panic disorder t1 (PHQ) (yes/no)	0.23	0.880	0.024	0.876	0.84	0.360	0.165	0.685
Asthma severity t2	38.02	<0.001	49.24	<0.001	39.64	<0.001	31.88	<0.001

PHQ: Patient Health Questionnaire; depressive disorder is both minor and major depression.

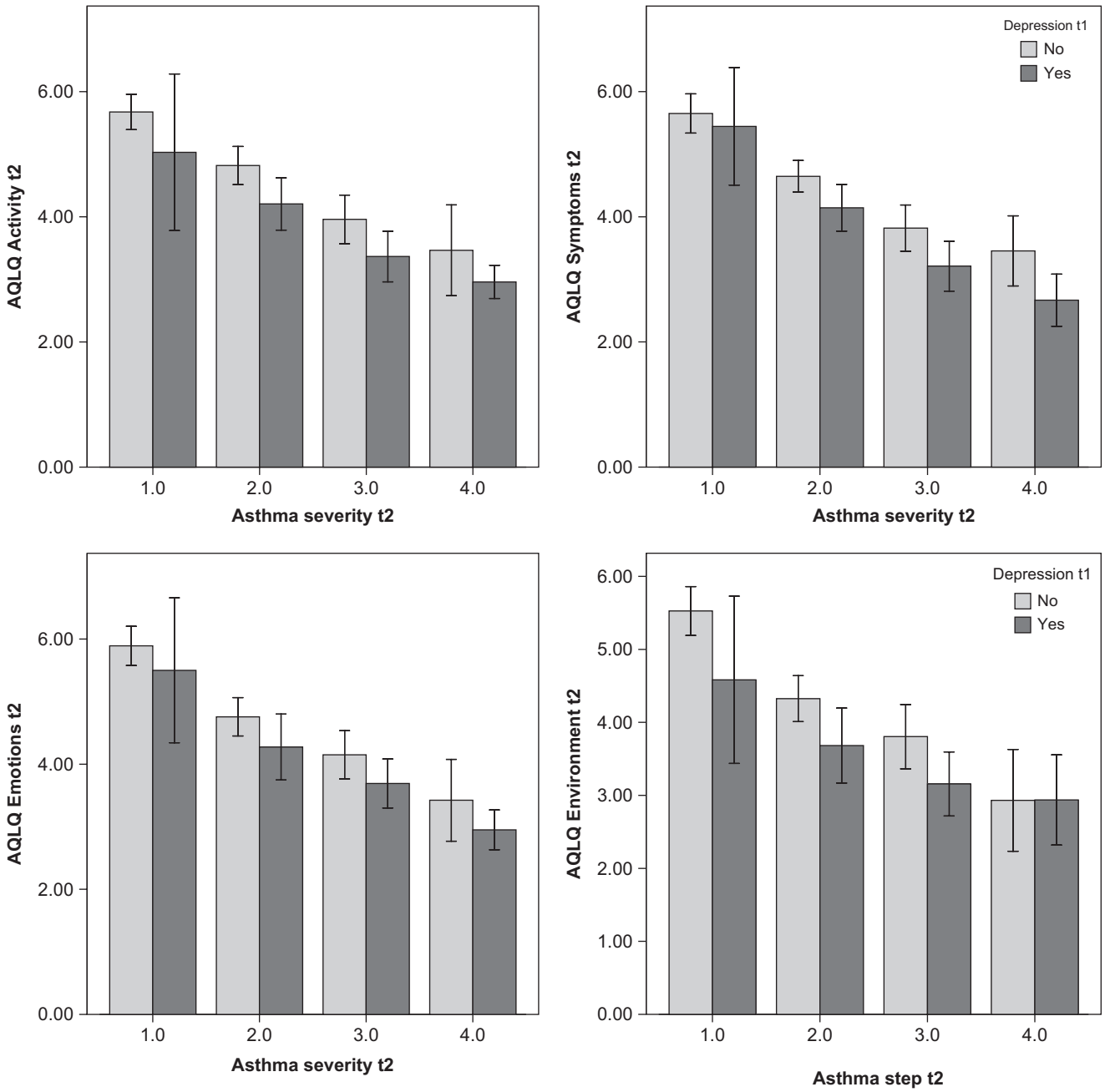

Figure 1 Scales of the Asthma Quality of Life Questionnaire (AQLQ) at follow up (t2) in patients with or without depression at baseline (t1). Values are mean (S.E.M.).

psychiatric comorbidity, in terms of depression. It remains to discuss why we did not find a relation between panic disorder and quality of life. An explanation might be that we used a diagnostic algorithm for panic disorder and did not use anxiety severity scores like other authors.[7,25]

A limitation of our findings was the low rate of hospitalisation, thus resulting in wide confidence intervals. This reflects reality in primary care, where the severity of a disease is generally lower than in specialised treatment settings,[45] which have also been shown to apply to asthma.[11] On the other hand, our results remain significant. Another aspect which could violate the generalisability of our study is the selection of patients. However, the responders and non-responders at follow-up did not differ with respect to asthma severity and the response rate was still 72%. Therefore, it seems unlikely that our results may overestimate the effect of depression and panic disorder. A further limitation of the study is that outcomes were completely based on patients self-reports. Although it has already been proven that the PHQ diagnostic algorithms result in realistic estimates for mood disorders, a standardised clinical interview would be a ''gold standard'' to confirm psychiatric diagnoses.[13] However, this was not possible due to the study design with the investigation of patients from 43 practices distributed over a broad area. Due to organisational reasons it was also impossible to

perform chart reviews to verify self-report information. Indeed, self-report information may be subject to recall bias. Another limitation of the study is that we accepted physicians' diagnoses without confirming them by broncho-provocation or by testing bronchodilator reversibility. However, the high number of patients taking steroids, which reflects ideal asthma therapy,[1] and the low number of smokers might indicate that we generated a coherent population. Nevertheless, if there were an overlap with COPD, the impact of psychiatric comorbidity remains substantial on this patient group.

Our findings highlight the impact of psychiatric comorbidity on asthma patient management in primary care. It could be worthwhile to focus not only on the somatic part of the disease but also to take into account the consequences of depression and panic disorder. However, it seems to be a challenge to address the needs of difficult asthma patients. One initial step to improving care could be to identify patients with high psychological comorbidity by analysing reasons for hospitalisation and emergency visits. In addition, psychotherapeutic or psychopharmacological treatment could be initiated. This might help to reduce unnecessary health care utilisation and to avoid associated potential harmful side effects (e.g. nosocomial infection in hospital or tachyarrhythmia due to intravenous theophylline). Finally, identification of these difficult patients could help physicians understand difficult doctor–patient interactions in situations where repeated home visits are requested with high emotional pressure. Therefore, actively involving the patients in order to facilitate empowerment could help both patients and doctors. Further research is necessary to find optimal strategies to deal effectively with asthma patients with high psychiatric comorbidity in general practice.

Conflict of interest statement

All authors declare that they have no conflict of interest.

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